a5 corrd. product. The sources of the genomic DNA samples for the different ethnic groups correspond to those previously described (Fernandez-Salguero *et al.* (1995) *Am. J. Hum. Genet.* 57: 651-660). --

Please insert the sequence listing, pages 1-5, at the end of the application.

IN THE CLAIMS:

Please cancel claims 12, 13, 14, 18, and 19. Please amend claims 1-11 and 15-17 as follows. Please add new claims 20-28 as follows.

Amend B1 1. (Amended) A method of detecting a splicing defect in a human dihydropyrimidine dehydrogenase gene, comprising determining whether a human genomic DNA encoding the human dihydropyrimidine dehydrogenase gene comprises a G residue at the position indicated as nucleotide 434 of SEQ ID NO: 1, wherein substitution of the G residue with an A residue causes a splicing defect in the human dihydropryimidine dehydrogenase gene.

2. (Amended) The method of claim 1, wherein the method comprises the step of amplifying human intronic dihydropyrimidine dehydrogenase genomic DNA which comprises a residue at the position indicated as nucleotide 434 of SEQ ID NO: 1.

a6 3. (Amended) The method of claim 2, wherein the method comprises amplifying the genomic DNA with a primer which hybridizes to a human dihydropyrimidine dehydrogenase genomic nucleotide sequence located within 500 nucleotides of the position indicated as nucleotide 434 of SEQ ID NO: 1.

4. (Amended) The method of claim 2, wherein the presence or absence of the G residue is detected by digestion of the amplified DNA with a restriction endonuclease.

5. (Amended). The method of claim 1, wherein the presence or absence of the G residue is detected by using an oligonucleotide array.

6. (Amended) A method of screening human patients for sensitivity to 5-fluorouracil, comprising isolating a genomic DNA from the patient and determining whether the genomic DNA comprises a G residue at the position indicated as nucleotide 434 of SEQ ID NO: 1.

Dep B1

7. (Amended) The method of claim 6, wherein the method comprises the step of amplifying human intronic dihydropyrimidine dehydrogenase genomic DNA from the patient which comprises a residue at the position indicated as nucleotide 434 of SEQ ID NO: 1.

8. (Amended) The method of claim 7, wherein the method comprises amplifying the genomic DNA with a primer which hybridizes to a human dihydropyrimidine dehydrogenase genomic nucleotide sequence located within 500 nucleotides of the position indicated as nucleotide 434 of SEQ ID NO: 1.

a6 cancel.

9. (Amended) The method of claim 7, wherein the presence or absence of the G residue is detected by digestion of the amplified DNA with a restriction endonuclease.

10. (Amended) A composition comprising a PCR primer which binds to a human dihydropyrimidine dehydrogenase intronic genomic nucleotide sequence located within 500 nucleotides of the position indicated as nucleotide 434 of SEQ ID NO: 1.

11. (Amended) The composition of claim 10, wherein the PCR primer binds to a human dihydropyrimidine dehydrogenase intronic genomic nucleotide sequence located within 100 nucleotides of the position indicated as nucleotide 434 of SEQ ID NO: 1.

Dep B2

15. (Amended) A kit comprising a container, a first PCR primer which binds to DNA 3' of a splice site in the human genomic DNA for an exon encoding amino acids 581-635 of human dihydropyrimidine dehydrogenase, and a second PCR primer which binds to DNA 5' of a splice site in the human genomic DNA for an exon encoding amino acids 581-635 of human dihydropyrimidine dehydrogenase, wherein at least one of the first or second PCR primers binds to a

a7 human dihydropyrimidine dehydrogenase intronic genomic nucleotide sequence located within 500 nucleotides of the position indicated as nucleotide 434 of SEQ ID NO: 1.

16. (Amended) The kit of claim 15, wherein the kit further comprises instructions for the detection of the presence or absence of a G residue in human dihydropyrimidine dehydrogenase genomic DNA at the position indicated as nucleotide 434 of SEQ ID NO: 1.

17. (Amended) The kit of claim 15, wherein the kit further comprises a restriction endonuclease which recognizes a sequence comprising a residue in human dihydropyrimidine dehydrogenase genomic DNA at the position indicated as nucleotide 434 of SEQ ID NO: 1.

20. (New) The method of claim 2, wherein the method comprises amplifying the genomic DNA with a primer which hybridizes to a human dihydropyrimidine dehydrogenase genomic nucleotide sequence located within 100 nucleotides of the position indicated as nucleotide 434 of SEQ ID NO: 1.

21. (New) The method of claim 4, wherein the restriction endonuclease recognizes a Mae II cleavage site.

22. (New) The method of claim 8, wherein the method comprises amplifying the genomic DNA with a primer which hybridizes to a human dihydropyrimidine dehydrogenase genomic nucleotide sequence located within 100 nucleotides of the position indicated as nucleotide 434 of SEQ ID NO: 1.

23. (New) The method of claim 9, wherein the restriction endonuclease recognizes a Mae II cleavage site.

24. (New) The kit of claim 15, wherein at least one of the first or second PCR primers binds to a human dihydropyrimidine dehydrogenase intronic genomic nucleotide sequence located within 100 nucleotides of the position indicated as nucleotide 434 of SEQ ID NO: 1.

25. (New) The kit of claim 17, wherein the restriction endonuclease recognizes a Mae II cleavage site.

26. (New) A kit comprising a container, a first PCR primer which binds to DNA 3' of a splice site in the human genomic DNA for an exon encoding amino acids 581-635 of human dihydropyrimidine dehydrogenase, a second PCR primer which binds to DNA 5' of a splice site in the human genomic DNA for an exon encoding amino acids 581-635 of human dihydropyrimidine dehydrogenase, and instructions for the detection of the presence or absence of a G residue in human dihydropyrimidine dehydrogenase genomic DNA at the position indicated as nucleotide 434 of SEQ ID NO: 1.